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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/603,478	06/24/2003	Adele L. Boskey	05983/100J990-US1	3518

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EXAMINER	
KWON, BRIAN YONG S	
ART UNIT	**PAPER NUMBER**
1614	

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08/06/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/603,478	BOSKEY ET AL.	
	Examiner	Art Unit	
	Brian S. Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05/07/2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24 and 29-34* is/are pending in the application.

4a) Of the above claim(s) *6,7 and 12-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5, 8-11, 24 and 29-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 June 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Acknowledgement is made of applicants' filing of the instant application as a Request for Continued Examination (RCE) under 37 CFR 1.1114.

2. Claims 1-5, 8-11, 24 and 29-34 are currently pending for prosecution on the merits.

3. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of actions being applied to the instant application.

Response to Arguments

4. Applicant's arguments filed 05/07/2007 have been fully considered but they are not persuasive.

Applicant's argument in the response takes the position that Boskey's gel system does not disclose a composition wherein all of the components of the claimed composition are present. Applicant argues that while rat skin collagen fibers are added to the system in Boskey, they are never added in combination with the complexed acidic phospholipids. Furthermore, applicant alleges that Boskey does not disclose or suggest the currently complex comprising a complexed acidic phospholipids and type I, type II or type IX collagen.

This argument is found unpersuasive. Unlike the applicant's argument, the scope of the instant invention encompasses not only the alleged complex comprising complexed acidic phospholipids and type I, type II and/or type IX collagen (where the collagen is complexed with the complexed acidic-phospholipid), but also the composition comprising complexed acidic phospholipids and type I, type II and/or type IX collagen (where the collage is not complexed

with the complexed acidic-phospholipid). Thus, the examiner maintains that Boskey's composition in gel system which contains synthetic complexed acidic phospholipids and fibrillar collagen, for example rat skin collagen, anticipates the claimed invention.

Even if assuming arguendo that the instant composition is limited to the complexed acidic-phospholipid-collagen (where the collagen is complexed with the complexed acidic-phospholipid), the examiner considers that the Boskey's composition also anticipates the claimed invention. As evidenced by the instant specification (Example 3, particularly page 17, lines 1-2), complexed acidic- phospholipid deems to have high binding affinity for rat collagen. Thus, it is clear that complexed acidic-phospholipid in Boskey's gel composition would form complexes with the rat skin collagen fibers.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, one would have been motivated to combine these references and make the modification because they are drawn to same technical fields, particularly utility of acidic-phospholipid complex (constituted with same ingredients and share common utilities), and pertinent to the problem which applicant concerns about. MPEP 2141.01(a).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1-5 and 8-11 are rejected under 35 U.S.C. 102(b) as being anticipated by A. Boskey (The Journal of Physical Chemistry, 1989, 93, 1628-1633).

The claims read on a composition comprising an acidic-phospholipid complex and collagen, wherein the complex comprises (i) calcium, namely calcium chloride, (ii) phospholipids, namely phosphatidylserine and (iii) inorganic phosphate, namely ammonium acid phosphate; and wherein the collagen is type I collagen, type II collagen, type IX collagen, or mixture thereof. Further limitations include "in molar ratio of 45-55 parts calcium:35-45 parts phospholipids:5-15 parts inorganic phosphate" (claim 2); "in a molar ratio range of 47-53 parts calcium:38-42 parts phospholipids: 8-12 parts inorganic phosphate" (claim 3); "in a molar ratio of 50 parts calcium: 40 parts phospholipids: 10 parts inorganic phosphate" (claim 5).

Boskey teaches a dynamic collagen gel system comprising synthetic complexed acidic phospholipids (see Boskey et al. (Calcif. Tiss. Res., 23, 251-258, 1977, particularly "Material and Methods" and "Results" for calcium-phospholipid-phosphate complex which comprises CaCl2, (NH4)2HPO4 and phospholipids: phosphatidyl serine, phosphatidyl inositol and phosphatidic acid, where calcium, phospholipid and inorganic phosphate is in a molar ratio range of 50 mol% (Ca): 40 mol% (phospholipids): 10 mol%(inorganic PO4) for your reference),

gelatin and fibrillar collagen, for example rat skin collagen. See abstract; page 1629, column 2, the last paragraph; and Tables II-III.

With respect to "type I collagen, type II collagen, type IX collagen or a mixture thereof" as a suitable gelatin in the instant invention, since there is no indication in the instant claim that said collagen must be essentially in purified or isolated form of "type I collagen, type II collagen, type IX collagen or a mixture thereof ", the referenced fibrillar collagen or rat skin collagen (inherently have type I, II and/or III collagen, see Danielsen, C., Biochem. J, 1982, 203, 323-326; Klein et al., Proct. Natl. Aca. Sci. USA, Vol. 74, No.4, pp. 1436-1439, 1977 for your reference), the examiner determines that Boskey's collagen gel system comprising complexed acidic-phospholipids, gelatin and fibrillar collagen anticipates the claimed invention.

Although Boskey does not specifically mention the presence of calcium chloride (CaCl2), ammonium acid phosphate (NH4)2HPO4 and phosphatidyserine, in a molar ratio range of 50 mol% (Ca): 40 mol% (phospholipids): 10 mol%(inorganic PO4), in said synthetic complexed acidic phospholipids, such ingredients in the claimed ratio must be inherently present in the referenced synthetic complexed acidic phospholipids. Therefore, the reference anticipates the claimed invention.

With respect to the intended use of said composition "for osteoinduction", such statement is not limited to the interpretation of composition claim. Thus, the reference anticipates the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 24 and 29-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jefferies (US 6311690) in view of Hollinger (US 4578384).

The claims read a method of inducing the growth of bone in mammal comprising administering complexed-acidic-phospholipid-collagen composite at a site in need of desired tissue growth. Further limitations include "bone growth" (claim 25); "the composite is in paste form, sponge form, molded form or preadsorbed onto an implant material" (claim 29); "the composite is encapsulated by an organic polymer" (claim 30); "further comprising one or more

materials selected from the group consisting of autologous osteoblasts, ondontoblasts, antibiotics, growth factors, cytokines and nanomaterials" (claim 32).

Jeffries teaches a collagen-calcium phosphate conjugate or a reconstituted collagen and acidic-phospholipids conjugate that is useful in inducing bone growth (Examples Twelve, Fifteen-Eighteen and Twenty-Eight), wherein said composition is administered in the form of implant material (column 1, lines 18-25; column 5, line 9); prepared in biopolymer organic matrix (column 5, lines 44-47 and column 7, lines 49-51); further comprises additional osteogenic factors, mitogens, drugs or antibiotics (abstract and claim 6). Jeffries also teaches the addition of biogenic component (i.e., acidic phospholipids or phospholipids) to increase tensile strength of said collagen-calcium phosphate particle conjugate (column 6, lines 13-43, particularly lines 35-36).

Hollinger is being supplied as a supplemental reference to demonstrate the use of biocompatible copolymer such as polyglycolic acid and polyactic acid in combination with acidic phospholipids complex for improving and promoting the healing of osseous tissue including bone, cementum and dentin (abstract; column 14, lines 28-32).

The teaching of Jeffries differs from the claimed invention in (i) the use of polyglycolic acid and the specific dosage amounts, namely "between about 5 mg and about 5g".

To incorporate such teaching into the teaching Jefferies, would have been obvious in view of Hollinger who teaches the use of biocompatible copolymer as secondary agent in preparing acidic phospholipids complex and the utility of acidic phospholipids complex composition in healing of osseous tissue including bone, cementum and dentin.

Although the instant claims use the different names for the said ingredients than those taught in the cited references, these references are particularly pertinent and relevant because all the claimed species and their roles are well taught in the cited reference. Thus, one would have been motivated to combine these references and make the modification because they are drawn to same technical fields (constituted with same ingredients and share common utilities), and pertinent to the problem which applicant concerns about. MPEP 2141.01(a).

With respect to the specific dosage amounts, namely "between about 5 mg and about 5g".

However, those of ordinary skill in the art would have been readily optimized effective dosages as determined by good medical practice and the clinical condition of the individual patient. Regardless of the manner of administration, the specific dose may be calculated according to body weight, body surface area or organ size. Further refinement of the calculations necessary to determine the appropriate dosage for treatment involving each of the above mentioned formulations is routinely made by those of ordinary skill in the art and is within the ability of tasks routinely performed by them without undue experimentation, especially in light of the dosage information and assays disclosed herein (Examples).

Relevant Art of Record

7. The prior art made of record and not relied upon is considered pertinent to applicant's invention. Please reference to Boskey et al. (Calcif. Tiss. Res., 23, 251-258, 1977 and Calcif. Tiss. Res., 1982, 34:S1-S7. Both reference discloses that synthetic calcium-phospholipid-phosphate complex comprises CaCl2, (NH4)2HPO4 and phospholipids: phosphatidyl serine,

phosphatidyl inositol and phsphatidic acid. Particularly, Boskey et al. (Calcif. Tiss. Res., 23, 251-258, 1977) discloses that calcium, phsopholipid and inorganic phosphate is in a molar ratio range of 50 mol% (Ca): 40 mol% (phospholipids): 10 mol%(inorganic PO4).

Conclusion

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached on (571) 272-0718. The fax number for this Group is (571) 273-8300.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications may be obtained from Private PAIR only. For more information about PAIR system, see http://pair-direct.uspto.gov Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Brian Kwon
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